Case Studies in Allergic Disease:

KEY DECISION POINTS IN DIAGNOSIS AND TREATMENT

THE THIRD IN A SERIES OF EDUCATIONAL NEWSLETTERS

PRESENTED BY:

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES OF THE NATIONAL INSTITUTES OF HEALTH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

IN COOPERATION WITH:

American Medical Association
Physicians dedicated to the health of America

American Academy of Allergy Asthma & Immunology

American Academy of Nurse Practitioners

American College of Occupational and Environmental Medicine

American Pharmacists Association
Improving medication use. Advancing patient care.

ACAAI
American College of Allergy, Asthma & Immunology

NAMCP
National Association of Managed Care Physicians
Taking the lead in assuring that physicians have a vital role in healthcare.

JOINTLY SPONSORED BY:

National Jewish Medical and Research Center
Global Leader in Lung, Allergic and Immune Diseases

IMED Communications LLC

THIS PROGRAM IS SUPPORTED BY AN UNRESTRICTED EDUCATIONAL GRANT FROM AVENTIS PHARMACEUTICALS

ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of National Jewish Medical and Research Center and IMED Communications. National Jewish Medical and Research Center is accredited by the ACCME to provide continuing medical education for physicians.

National Jewish Medical and Research Center designates this educational activity for a maximum of 1 category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits he/she actually spent in the activity.

TARGET AUDIENCE

Allergists/Immunologists, Pulmonologists, General Practitioners, Internists, Pediatricians, Otolaryngologists, Dermatologists, and Allied Healthcare Professionals.

STATEMENT OF NEED

Allergic diseases, including allergic rhinitis, latex allergy, food allergy, drug allergy, insect-sting allergy, urticaria, and atopic dermatitis, affect a substantial proportion of the US population, and their incidence is increasing. Some of these reactions can be fatal if untreated or improperly treated, and the most common of all allergic reactions, allergic rhinitis, can contribute to more serious and difficult-to-treat conditions such as otitis media, sinusitis, and asthma. Despite their rising frequency and potentially serious consequences, allergic disorders are commonly unrecognized, and even the cases that are diagnosed correctly are often treated suboptimally. These facts underscore the need for comprehensive contemporary educational activities for healthcare professionals in the identification and management of allergies. This mandate is supported by consultation with leading experts in allergic disease, a review of the current literature, and the results of surveys conducted at prior symposia.

Program Chairs

Erwin W. Gelfand, MD
Chairman, Department of Pediatrics
Division of Cell Biology
National Jewish Medical and Research Center
Denver, CO

Marshall Plaut, MD
Chief, Allergic Mechanisms Section
Division of Allergy, Immunology, and Transplantation
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD

CME Planning/Steering Committee

Erwin W. Gelfand, MD
Chairman, Department of Pediatrics
Division of Cell Biology
National Jewish Medical and Research Center
Denver, CO

Marshall Plaut, MD
Chief, Allergic Mechanisms Section
Division of Allergy, Immunology, and Transplantation
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD

Terry Washington
Project Coordinator
Office of Professional Education
National Jewish Medical and Research Center
Denver, CO

Disclosures

The Continuing Medical Education (CME) committee at National Jewish Medical and Research Center complies with the Standards for Commercial Support of Continuing Medical Education adopted by the American Council for Continuing Medical Education (ACCME). Our goal is to ensure that there is no compromise of the ethical relationship that exists between those in charge of the program and those attending the program and their respective professional duties.

"Significant Financial Interest" is defined as:

- Presently owning a major block of stock in the company (direct ownership)
- Having received honoraria or consultation fee from the company within the past 2 years
- Having received a research grant from the company within the past 2 years

Unless indicated on the following speaker list, none of the faculty has indicated "Significant Financial Interest" in a company. The following faculty have stated they have received grant/research support from, have been consultants/scientific advisors for, have been on the speakers bureau of, and/or have had other financial interest relationships with manufacturers of any commercial products as indicated below.

Faculty

Fred McDaniel Atkins, MD 11, 21, 30, 41, 56, 61
Medical Director
Pediatric Day Program
National Jewish Medical and Research Center
Denver, CO

Ronald C. Balkissoon, MD 11, 19, 30, 46, 56
Associate Professor
Division of Environmental and Occupational Health Sciences
National Jewish Medical and Research Center
Denver, CO

Leonard Bielory, MD 12, 27, 41, 43, 46, 47
Professor of Medicine, Pediatrics and Ophthalmology
Director, Division of Allergy, Immunology and Rheumatology
UMDNJ – New Jersey Medical School
Newark, NJ

Michael S. Blaiss, MD 11, 12, 30, 41, 46
Clinical Professor of Pediatrics and Medicine
University of Tennessee Health Science Center
College of Medicine
Memphis, TN

Mark Boguniewicz, MD 12, 28, 46
Professor, Division of Pediatric Allergy-Immunology
Department of Pediatrics
National Jewish Medical and Research Center and University of Colorado School of Medicine
Denver, CO

Joshua A. Boyce, MD 30, 41, 42
Assistant Professor of Medicine
Harvard Medical School
Associate Director of Research in Inflammation and Allergic Disease
Brigham and Women's Hospital
Boston, MA

David H. Broide, MB, ChB 30, 49, 60
Professor of Medicine
University of California, San Diego
La Jolla, CA

Thomas B. Casale, MD 6, 7, 11, 12, 18, 20, 27, 29, 32, 41, 43, 46, 48, 49, 54, 57, 63, 65, 69
Creighton University
Department of Medicine
Chief, Allergy/Immunology
Professor of Medicine
Creighton University
Omaha, NE

Erwin W. Gelfand, MD 12, 17, 41
Chairman, Department of Pediatrics
Division of Cell Biology
National Jewish Medical and Research Center
Denver, CO

Guenther Hochhaus, PhD 1, 11, 12, 37, 57
University of Florida
Department of Pharmaceutics
Gainesville, FL

Eli O. Meltzer, MD 1-5, 8, 10-15, 19-22, 24-27, 29-31, 33-36, 38-46, 48-50, 53, 55-59, 62, 64, 66-68, 70
Co-Director
Allergy & Asthma Medical Group & Research Center
Clinical Professor of Pediatrics
University of California, San Diego
San Diego, CA

David P. Skoner, MD 12, 30, 41, 56, 57
Director, Division of Allergy, Asthma, and Immunology
Department of Pediatrics
Vice Chairman for Clinical Research
Allegheny General Hospital
Allegheny, PA

Alkis Togias, MD 5, 11, 16, 30, 41, 49, 56
Associate Professor
Johns Hopkins University
Johns Hopkins Asthma and Allergy Center
Baltimore, MD

Discussants

Berrylin J. Ferguson, MD 11, 12, 20, 30, 41, 49, 56, 66
University of Pittsburgh School of Medicine
Pittsburgh, PA

Leonard Fromer, MD, FAAFP, FABFP *
UCLA School of Medicine
Santa Monica, CA

Mary Lou Hayden, RN, MS, FNP-C, AE-C
University of Virginia 11, 12, 29, 41, 46, 49
Richmond, VA

Christopher G. Massey, PA-C, RRT 12, 30
Asthma & Allergy Physicians
Brockton, MA

Michael Toscani, PharmD 9, 52
Senior Consultant, Health Answers
Rutgers University College of Pharmacy
Titusville, NJ

Barbara P. Yawn, MD, MSc 23, 56
Olmstead Medical Center
Rochester, MN

Commercial Company

1. 3M Pharmaceuticals
2. Abbott Laboratories
3. Aerogen, Inc.
4. Agouron Pharmaceuticals, Inc.
5. Alcon Laboratories Inc.
6. Alkermes, Inc.
7. Allergenics
8. Almirall Prodesfarma, S.A.
9. Amgen, Inc.
10. Arris Pharmaceutical Corporation
11. AstraZeneca Pharmaceuticals LP
12. Aventis Pharmaceuticals
13. Axys Technologies, Inc.
14. Baker Norton Pharmaceuticals, Inc.
15. Bausch & Lomb
16. Baxter Healthcare Corporation
17. Bayer Corporation
18. Biogen, Inc.
19. Boehringer Ingelheim Pharmaceuticals, Inc.
20. Bristol-Myers Squibb
21. Dey, Inc.
22. Dura Pharmaceuticals
23. Eli Lilly and Company
24. Entelos, Inc.
25. Ferraris Group PLC
26. Flemington Pharmaceutical Corporation
27. Forest Laboratories, Inc.
28. Fujisawa Healthcare, Inc.
29. Genentech, Inc.
30. GlaxoSmithKline
31. Hoffmann-La Roche Ltd.
32. IDEC Pharmaceuticals Corporation
33. Immunex Pharmaceuticals
34. Inspire Pharmaceuticals, Inc.
35. Janssen Pharmaceutica
36. Kos Pharmaceuticals, Inc.
37. Mano-therapeutics
38. Mast
39. McNeil Consumer & Specialty Pharmaceuticals
40. Medeva Pharma
41. Merck & Co., Inc.
42. Millennium Pharmaceuticals, Inc.
43. Muro Pharmaceutical, Inc.
44. Nastech Pharmaceutical Co., Inc.
45. National Institutes of Health
46. Novartis Pharmaceuticals Corporation
47. Otsuka America Pharmaceuticals, Inc.
48. Parke-Davis
49. Pfizer Inc.
50. Pharmacia & Upjohn
51. Protein Design Labs, Inc.
52. Purdue Pharma L.P.
53. Rigel Pharmaceuticals, Inc.
54. Sankyo Corporation
55. Sanofi-Synthelabo Inc.
56. Schering-Plough Corporation
57. Sepracor Inc.
58. State of California
59. Synergen, Inc.
60. Taisho Pharmaceutical Co., Ltd.
61. Tanox, Inc.
62. TAP Pharmaceuticals Inc.
63. Toray Industries, Inc.
64. UCB Pharma, Inc.
65. ViroPharma Inc.
66. Wallace Pharmaceuticals
67. Warner-Lambert Company
68. Whitehall-Robins Inc.
69. Wyeth Healthcare Products
70. Zambon Group

* Has indicated no financial interest or other relationship with any manufacturer of any commercial products.

Interdisciplinary Medicine®

OCTOBER 2003 VOL. 5 NO. 3

Release date:
October 2003

Expiration date:
October 2004

Case Studies in Allergic Disease: Key Decision Points in Diagnosis and Treatment

INTRODUCTION: MEETING THE NEEDS OF PATIENTS WITH ALLERGIC REACTIONS

Allergic rhinitis (AR), urticarial skin reactions, and atopic dermatitis (AD) are among the most common manifestations of the atopic predisposition, yet they often present diagnostic and therapeutic difficulties, even for an experienced clinician. Each has a broad range of causes or triggers, which may or may not be readily identifiable. Their clinical presentations can vary widely between patients and even between different episodes in the same patient, and the symptoms are not always specific or pathognomonic. Even when the reactions are identified correctly, many obstacles can stand in the way of effective treatment, including wide interpatient variability in drug response and tolerability, the difficulty of adhering to complex regimens, and the limitations of insurance coverage for prescription drugs. Diagnosis and treatment are complicated further by the unique medical needs of children, who constitute a high proportion of patients with these allergic disorders.

Contemporary strategies for overcoming these difficulties were presented and discussed at a roundtable conference entitled, "Current Trends in Allergic Reactions: A Multidisciplinary Approach to Patient Management," held in Bethesda, Maryland, on February 10 and 11, 2003. The conference was presented by the National Institute of Allergy and Infectious Diseases, a division of the National Institutes of Health, and was sponsored by National Jewish Medical and Research Center in Denver, Colorado. The faculty, co-chaired by Erwin Gelfand, MD, and Marshall Plaut, MD, included a group of allergists, primary care physicians, an otolaryngologist, immunologists, a nurse practitioner, a physician assistant, and a pharmacist. This newsletter presents 3 case studies that illustrate strategies delineated by the panel for identifying the causes of allergic reactions, managing the symptoms, and helping patients avoid further allergen exposures. Each case highlights important decision points in patient care, with a focus on developing treatment plans that are effective, safe, well tolerated, cost-conscious, and acceptable to patients over the long term. The conference and newsletter were made possible by an unrestricted educational grant from Aventis Pharmaceuticals.

Educational Objectives

After reading this newsletter, clinicians should be able to:

- Discuss the clinical presentations of allergic rhinitis, urticaria, and atopic dermatitis
- Recognize the advantages and limitations of diagnostic tests for allergic disease
- Counsel patients on how to minimize their exposure to the triggers of allergic rhinitis, urticaria, and atopic dermatitis
- Understand how drug treatments affect allergy symptoms, daily functioning, quality of life, and adherence
- Describe the role of food and latex allergies in chronic urticaria

CASE 1: A 15-YEAR-OLD AVID SPORTSMAN

Patient Presents

- **Persistent anterior rhinorrhea**
- **Sneezing spasms**
- **Chronic nasal congestion**
- **Ocular itching and tearing**
- **Exercise-induced chest tightness**

Case Presentation

An adolescent boy is brought in by his mother for evaluation of respiratory symptoms. His complaints include persistent anterior rhinorrhea, sneezing spasms, chronic nasal congestion, ocular itching

Interdisciplinary Medicine®

This *Interdisciplinary Medicine®* is presented by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health. It is sponsored by National Jewish Medical and Research Center and IMED Communications in cooperation with the American Academy of Allergy, Asthma & Immunology; the American Academy of Nurse Practitioners; the American Academy of Otolaryngic Allergy & Foundation; the American Academy of Physician Assistants; the American College of Allergy, Asthma & Immunology; the American College of Occupational and Environmental Medicine; the American Medical Association; the American Pharmacists Association; and the National Association of Managed Care Physicians.

This *Interdisciplinary Medicine®* is published under an unrestricted educational grant from Aventis Pharmaceuticals. This newsletter was developed and produced by IMED Communications. The publishers reserve copyright on all published materials, and such material may not be reproduced in any form without written permission of IMED Communications.

For additional continuing medical education opportunities related to this subject, visit the National Institute of Allergy and Infectious Diseases of the National Institutes of Health Web site at: http://www.niaid.nih.gov/research/dait.htm.

Please direct all correspondence to:
Editor, *Interdisciplinary Medicine®*
IMED Communications
Department 102
Suite 200
518 Route 513
PO Box 458
Califon, NJ 07830

and tearing, and exercise-induced chest tightness. He is an avid participant in outdoor sports in spring, summer, and fall, and he reports that the symptoms greatly interfere with his athletic performance and enjoyment. Constant rubbing and wiping have caused sores to develop around his nose, which he finds unattractive and embarrassing. These quality-of-life issues are very typical of AR in his age group: In a study of 83 adolescents with allergic rhinoconjunctivitis, quality of life was impaired not just because of nasal and ocular symptoms but also because of poor concentration, fatigue, irritability, embarrassment, and limitations in outdoor activities.[1] Similarly, a survey of 1458 Swedish teenagers with self-reported allergic rhinoconjunctivitis found that more than half felt tired and unattractive because of the symptoms, which they considered very distressing.[2] The discomfort and sleep disruption caused by allergic symptoms often make adolescents feel unmotivated, forgetful, and disinterested in daily activities, and their classroom performance suffers as a consequence.[1,3,4]

Decision Points for Diagnosis

This boy's extensive participation in outdoor sports during pollen season strongly implicates outdoor allergens as a cause. He has no pets, so animal dander is probably not a culprit allergen. The first question in confirming the diagnosis is whether to evaluate him for allergen sensitivity. Given his chest tightness on exercise, another diagnostic test to consider is pulmonary function assessment before and during exercise. Because adolescent boys may understate or downplay symptoms of illness, it is important to make an objective assessment of this boy's chest symptoms and treat them vigorously if needed.

The boy and his mother agree to allergy testing, which reveals prominent reactions to grasses and weeds and moderate reactions to trees and dust mites. The initial treatment recommendations consist of allergen-avoidance measures such as keeping the boy's bedroom windows closed, using an air conditioner with an allergen-trapping filter, covering his pillow and mattress with cases that are impermeable to dust mites, and removing an old carpet from his room. It is important to note that the standard metal mesh screen on most air conditioners may not trap airborne allergens; pleated paper filters or specially designed allergen-trapping filters should be used instead (although they are likely to be more expensive).

Decision Points for Drug Therapy

Avoidance measures are unlikely to control this child's symptoms fully, so drug therapy is warranted. A logical first choice would be to try a nonsedating antihistamine that can be taken once or twice daily, such as fexofenadine, loratadine, or desloratadine.[5] Because AR itself often causes daytime fatigue and learning impairment,[3,6,7] it is important to choose an agent that will not worsen these effects. Fexofenadine (Figure 1) and loratadine have been shown to improve school performance in youngsters with AR, whereas sedating agents such as diphenhydramine worsen their learning ability even more than AR itself does.[4,7] Controlling upper-airway symptoms with a nonsedating antihistamine may have the additional benefit of improving the boy's lower-airway function,[8,9] but his symptoms are too severe to be controlled by antihistamines alone.

Treatment Options

- **Allergen-avoidance measures**
- **Nonsedating antihistamine**
- **Leukotriene modifier**
- **Intranasal corticosteroid**
- **Inhaled corticosteroid**
- **Decongestant**

Leukotriene modifiers are another option for treating this patient's AR symptoms. However, a recent comprehensive literature review concluded that they are not superior to second-generation antihistamines in terms of relieving congestion or other nasal symptoms and hence offer no unique benefits in the treatment of AR for patients with or without comorbid asthma.[10,11] There is little evidence that an antihistamine plus a leukotriene modifier is any more effective than an antihistamine alone would be.[10,12]

This patient's symptoms are so severe and persistent that he will most likely need to be prescribed an intranasal corticosteroid, as recommended by the Allergic Rhinitis Impact in Asthma (ARIA) guidelines.[13] Regarding patients with perennial AR, head-to-head comparisons have shown no marked differences between intranasal steroids in safety or efficacy.[14,15] These agents are highly effective in controlling nasal and ocular symptoms, more so than leukotriene receptor antagonists.[10] In general, intranasal steroids do not have a pronounced effect on growth velocity in children, but there may be some differences within the class. For example, a year-long study of

98 prepubertal children with perennial AR showed that mometasone 100 mcg/day had no effect on growth,[16] whereas another year-long study of 100 children found that beclomethasone 336 mcg/day slowed growth by about 0.9 cm/y compared with placebo.[17] Prescribers should bear in mind that adolescents may not find nasal sprays acceptable: This study revealed that many refused to use intranasal medications daily because of inconvenience and embarrassment.[2]

If this patient's pulmonary-function testing suggests the presence of asthma, and control of his nasal symptoms does not alleviate his pulmonary complaints completely, he may also benefit from regular use of an inhaled corticosteroid. In addition, using an inhaled bronchodilator immediately before exercise may help relieve his sensations of chest tightness. Because of concerns about the long-term course of asthma, including the potential for airway remodeling,[18] it is particularly important to evaluate the child's pulmonary symptoms fully and treat them aggressively if necessary.

Since chronic nasal congestion is among this boy's most troublesome complaints, it may be necessary to add a decongestant to his regimen. Pseudoephedrine is effective and safe when used in combination with a nonsedating antihistamine such as fexofenadine.[19,20] Another possible addition to the treatment plan might be a nasal and/or ocular mast cell stabilizer, although teenagers often find these delivery forms embarrassing or awkward to use.

In selecting therapy for adolescents, clinicians should anticipate their difficulties in adhering to complex regimens. A treatment plan that involves taking several different drugs several times per day may not be realistic for a teenager over the long term, especially one with a busy recreational schedule. If the family's healthcare plan does not cover all the costs of prescriptions, their ability to afford co-payments for multiple drugs should also be considered.

Long-Term Care and Follow-up

The boy should return to his physician's office about 3 to 6 months after his symptoms have been brought under control so that his physician can monitor his response and adjust his therapy if needed. If it is determined that his symptoms are mostly intermittent or seasonal, the clinician may consider eliminating some medications in the winter months to make the regimen simpler and more affordable.

Referral to a specialist for allergen immunotherapy should also be discussed with the boy and his family. Immunotherapy may be effective in controlling symptoms caused by animal dander, dust mites, and pollen, and the benefits may be sustained even after therapy is discontinued.[21] Recent evidence suggests that immunotherapy not only may reduce the symptoms of AR and allergic asthma but also could prevent the progression to asthma that is frequently observed in patients with AR.[21,22]

CASE 2: A 40-YEAR-OLD MAN WITH LATEX ALLERGY

Patient Presents

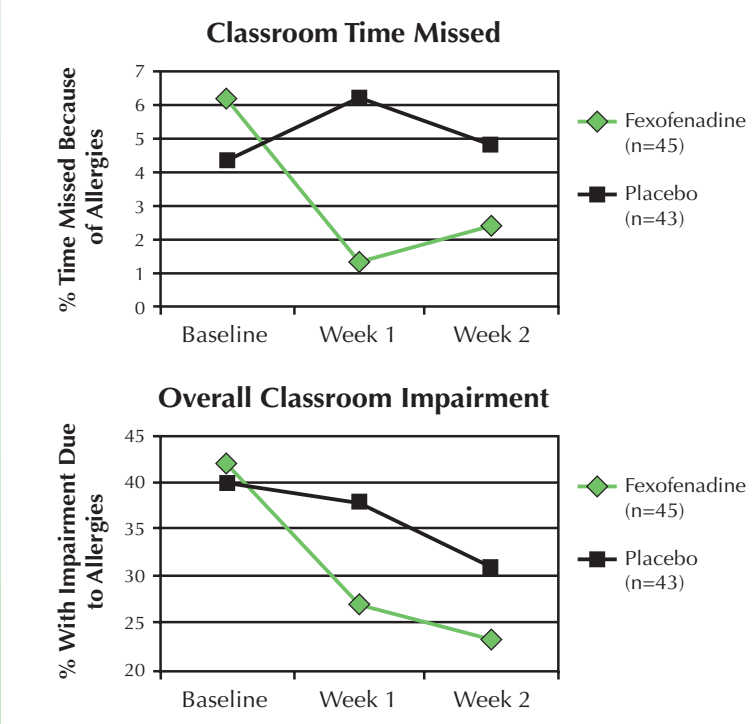
- **Generalized urticaria**
- **Rhinoconjunctivitis**
- **Periorbital edema**

Case Presentation

A man presents for follow-up after experiencing a severe episode of anaphylaxis during preparations for his young son's birthday party. He reports that

FIGURE 1

Effects of Fexofenadine 60 mg BID Versus Placebo on Classroom Time Missed and Self-Reported Overall Impairment in the Classroom in 88 Students With Seasonal AR. Differences Between Fexofenadine and Placebo Were Significant at Week 1 ($P \leq 0.05$)



Adapted with permission from Tanner LA, et al. *Am J Managed Care*. 1999;5(suppl):S244-S247.

he developed generalized urticaria, rhinoconjunctivitis, and periorbital edema; the symptoms worsened rapidly in that his breathing became very difficult and he became so light-headed that he could not stand up. The episode resolved only after he received subcutaneous epinephrine in the emergency department.

Initial Treatment Options

- **Latex avoidance**
- **Self-administered epinephrine**

According to his occupational history, he had been a schoolteacher for most of his career but switched jobs about 2 years ago to become a medical laboratory technician. When he is asked about any other respiratory symptoms, he admits to mild coughing and wheezing at his workplace in the past few months, although he has not felt that it was serious enough to necessitate medical care. He reports that he and all of his laboratory coworkers wear gloves when handling biological specimens. He has no history of allergies, but upon questioning, he recalls a transient episode of generalized itching after using a condom some months ago. Further inquiry reveals that the recent episode of anaphylaxis occurred immediately after the patient inflated latex party balloons.

Decision Points for Diagnosis

The patient's history strongly suggests the possibility of latex allergy. Sensitization to certain proteins in natural rubber latex is far more common among workers in the healthcare and biomedical industries than in the general population, probably because of the frequent use of latex gloves and other materials as part of the universal precautions against infection.[23-25] Sensitization occurs through physical contact with and/or inhalation of powder containing these proteins—in fact, latex-related occupational asthma is almost exclusively caused by powdered latex gloves.[24,25] The fact that this patient's symptoms did not develop immediately after he became a laboratory technician does not rule out latex allergy as a possible diagnosis: A survey of 63 individuals with latex allergy found an average latency of 5 years between the start of occupational exposure to latex products and the emergence of symptoms. In almost all of these individuals, the first sign of allergy was contact urticaria, accompanied in some cases by rhinitis or dyspnea.[23]

Modified Treatment Options

- **Elimination diet**
- **Written action plan for accidental exposure**
- **Bronchodilator**

The first decision point is whether to perform skin testing and/or radioallergosorbent testing (RAST) for latex allergy and, possibly, for other allergens as well. The patient refuses skin testing, but the results of RAST are strongly positive for latex-specific immunoglobulin E (IgE). RAST for several food allergens and some aeroallergens are positive but less strongly so than for latex. This is not surprising, as latex-allergic individuals are usually atopic and thus would be expected to have positive results on tests for multiple allergens.

Decision Points for Treatment

The initial treatment recommendation for this patient is avoidance of latex products at home and in the workplace. He is given a prescription for self-administered epinephrine and detailed education on how and when to use it. After he persuades his supervisor at work to switch to powder-free, low-protein synthetic gloves, his respiratory symptoms improve somewhat. This is consistent with research showing that removing latex aeroallergens from the workplace can reduce allergies and asthma, although the benefits may take 1 or 2 years to become apparent.[24,26,27]

Emergence of Cross-Reactivity

The patient returns to his physician's office 1 month later after experiencing symptoms of urticaria, periorbital edema, and rhinoconjunctivitis during an office party. He was able to control the symptoms somewhat by using his epinephrine autoinjector, but he required further stabilization in the emergency department. An algorithm for the treatment of anaphylaxis is shown in Figure 2. The patient denies contact with latex balloons or any other latex products at the party and worries that the initial diagnosis was wrong. When asked about what foods were served at the party, he recalls that they included guacamole dip, tacos, and fruit salad, all of which he had eaten uneventfully at other times in his life.

He now consents to skin testing, which shows strong positive reactions to latex, avocado, and kiwi. Latex allergy frequently coexists with allergies to these fruits, as well as to plum, nectarine, melon, banana, and papaya, among others.[28-30] In this case, the food allergies appear to have emerged after the latex sensitization. While weakly positive RAST tests are difficult to interpret, the weakly positive RAST to foods in this latex-allergic man, 1 month earlier, raises the possibility of sensitivity to food. Skin testing is often more sensitive than RAST, and the strongly positive skin test reactions to foods confirm the clinical reaction to the fruits.

The patient's treatment plan is modified to include an elimination diet, a written action plan for accidental exposures, and regular reinforcement of the importance and correct use of self-injected epinephrine. Even patients who are carefully instructed in the use of epinephrine autoinjectors tend to forget how to use them and may neglect to carry them with them if they have not had reactions in some time. Patients who know what they are allergic to are particularly prone to this type of complacency, because they believe they can simply avoid the offending substance. The unpredictability of exposures and the life-threatening nature of the reactions must be strongly emphasized in patient counseling.

Decision for Further Evaluation and Treatment

The foundation of treatment in a case such as this is instructing the patient to avoid potential triggers meticulously and arming him with treatments he can administer himself. Additional steps to consider include referral to a dietitian for further advice about the elimination diet. A food challenge to confirm his sensitivity is unnecessary at this stage and is potentially dangerous, but it may be advisable to monitor him at specified intervals for changes in his allergen sensitivity. Finally, it may be worthwhile to evaluate him for latex-induced asthma, because anaphylaxis is more likely to be fatal to asthmatic than to nonasthmatic individuals. If his lung function is impaired, a bronchodilator should be added to his emergency self-treatment kit. At this time, immunotherapy for latex allergy is still investigational and cannot be recommended routinely.

CASE 3: A 3-YEAR-OLD GIRL WITH A SEVERE RASH

Patient Presents

- **Pruritic rash on face and outer limbs**
- **Recurrent skin infections**
- **Severe eczematous rash with erythematous papules with serous exudate and thick, lichenified plaques**
- **Skin widely excoriated because of scratching**
- **Areas on face with signs of secondary bacterial infection**

Case Presentation

A 3-year-old girl is brought in by her parents for evaluation of an intensely pruritic rash on her face and outer limbs accompanied by recurrent skin infections. Her parents report that the symptoms have been present since her infancy but have worsened markedly in recent months. Physical examination shows a severe eczematous rash characterized by erythematous papules with serous exudate and thick, lichenified plaques. The child's skin is widely excoriated because of scratching, and, in fact, she is unable to refrain from vigorous scratching even during the brief examination. Many areas on her face and extremities show signs of secondary bacterial infection.

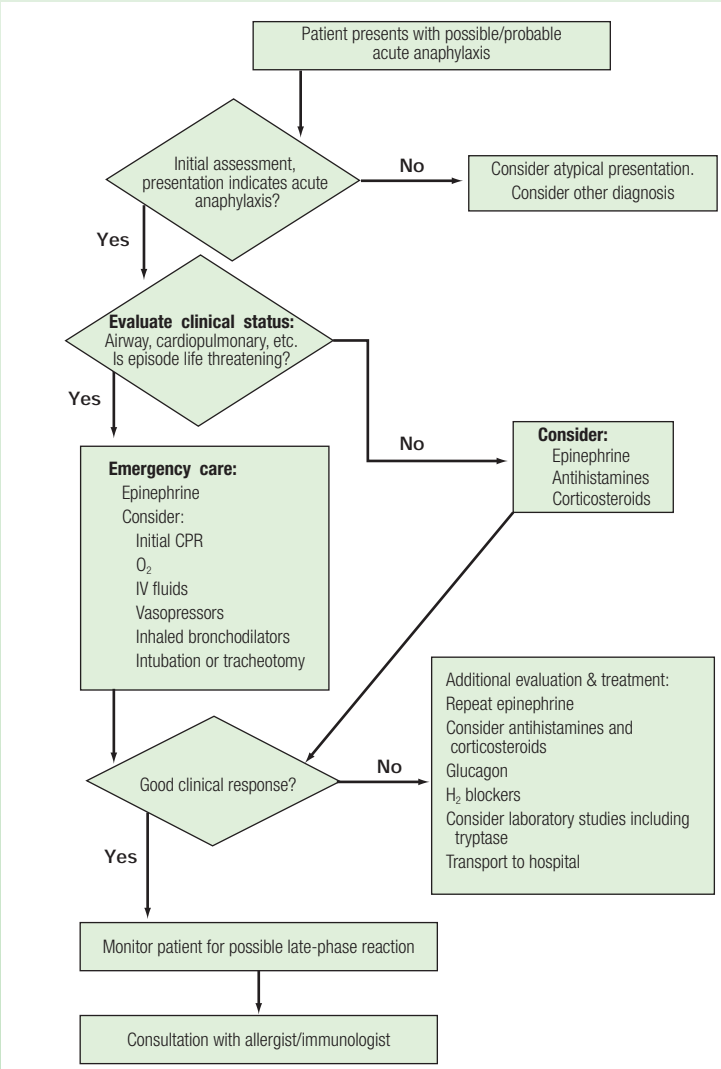
The girl's parents describe the itching as being worst at night, disrupting sleep for the entire family. They are clearly exhausted and distressed, having rarely had an uninterrupted night of sleep since their daughter was born. Her symptoms are so severe that her day care center often refuses to allow her to stay, resulting in lost work time for the parents and a sense of social ostracization for the child.

Decision Points for Diagnosis

The first decision point is what diagnostic tests to perform; the options include skin-prick testing, RAST for common food and airborne allergens, and tests to rule out other conditions in the differential diagnosis, such as impetigo. The family history is clearly significant: Both parents demon-

FIGURE 2

Algorithm for the Management of Anaphylaxis



Adapted from *J Allergy Clin Immunol.*, Vol 101, Nicklas RA. The diagnosis and management of anaphylaxis, pages S465-S528, Copyright 1998, with permission from American Academy of Allergy, Asthma, and Immunology.

strate sensitivities—the father has seasonal allergic rhinitis in reaction to timothy grass pollen, and the mother has asthma and is allergic to house dust mites and ragweed.

Initial Treatment Options

- **Strict avoidance of identified allergens and exacerbating factors**
- **Referral to dietitian**
- **Daily soaking baths followed by application of emollients**
- **Topical corticosteroid**
- **Oral antihistamine**

The girl's parents agree to skin tests, which show strongly positive results for milk, egg, corn, soy, dust mite, and cat allergens. Based on the distribution and duration of the rash and the personal and family evidence of atopy, a presumptive diagnosis of AD is made.[31] The onset of this chronic, relapsing, inflammatory skin disease usually occurs in the first year of life, and the typical triggers include foods and aeroallergens (Table 1).[32,33] As this patient's family circumstances show, the intense itching and cutaneous hyperreactivity can severely impair quality of life for both patients and their caregivers.[32,33]

Although the pathophysiology of AD is still under investigation, most available evidence points to immune dysregulation in the form of an exaggerated systemic T_H2 response. Whereas T_H1 cytokines predominate in chronic AD lesions, T_H2 cytokines are increased in acute lesions.[34] In addition, levels of circulating eosinophils and serum IgE are elevated in patients with AD, as is the spontaneous release of histamine from basophils, whereas the expression of interferon (IFN)-γ-secreting T_H1 cytokines is depressed.[32,35] Recent evidence suggests that some cases may represent abnormal responses to bacterial or fungal skin infections. For example, *Staphylococcus aureus* is found in more than 90% of AD lesions compared with only 5% of skin samples from healthy subjects, and some patients obtain relief from antistaphylococcal agents, even in the absence of secondary bacterial infections. The culprit agents are thought to be certain staphylococcal toxins, which act as superantigens to activate T cells and macrophages. In other cases, patients are sensitized to certain fungi and show responses to antifungal therapy. Autoimmune mechanisms may also play a role in some reactions.[32]

Initial Treatment Recommendations

Modified Treatment Options

- **Topical calcineurin inhibitor**
- **Reduction in topical corticosteroid**

The approach to treating AD is usually multifaceted, beginning with strict avoidance of identified allergens and exacerbating factors such as skin irritants, infections, and emotional stress. Because the patient is allergic to several basic foods, the parents are referred to a dietitian for guidance to ensure that her daily food intake is nutritionally adequate. The parents are also advised to give the child a soaking bath each day followed by an application of emollients. Topical corticosteroids are recommended to control her skin inflammation, but the courses should be kept short because of the risk of side effects such as skin atrophy. In addition, an oral antihistamine is prescribed to alleviate her pruritus.[32]

The girl is brought in several weeks later for a follow-up visit. She shows a partial response to initial treatment, but neither her physician nor her parents consider it fully adequate. The mother admits that she occasionally hesitates to use the topical corticosteroids because of concerns about their long-term safety. The physician elects to add a topical calcineurin inhibitor to the patient's regimen. This novel, nonsteroidal class of therapy for AD has multiple anti-inflammatory effects that produce rapid symptom control, reduce the number of flare-ups (Figure 3), decrease the need for steroids, and suppress staphylococcal skin colonization.[32,36,37] Calcineurin inhibitors are not associated with the side effects typical of steroids, and 2 members of the class, tacrolimus and pimecrolimus, are approved for patients as young as 2 years of age. They are currently used as substitutes for or adjuncts to steroids.

Table 1

Common Triggers of Atopic Dermatitis

Foods	Aeroallergens
Egg	Dust mites
Milk	Pollens
Wheat	Animal danders
Soy	Molds
Peanuts	

Leung DY. *J Allergy Clin Immunol*. 2000;105:860-876.

One month later, the parents describe dramatic resolution of the child's symptoms, which is confirmed on physical examination. Scarring from the secondary bacterial infections is minimal. The parents also report a profound improvement in quality of life for the child and her entire family. She is regaining the social skills she had lost during her long isolation from other children, and both she and her parents are noticeably more rested and relaxed than at their previous visits.

Long-Term Care and Follow-up

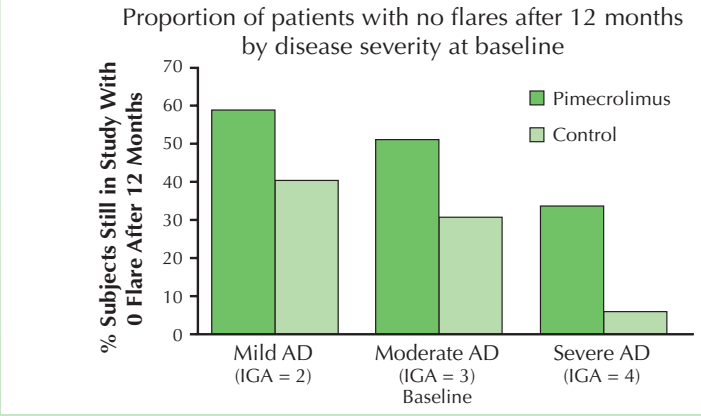
Long-term care for this child rests on periodic visits to monitor her response to treatment and adjustments to the treatment plan if needed. The severity of AD often diminishes in late childhood.[33] Because many patients are left with a predisposition toward skin diseases such as chronic xerosis and occupational hand dermatitis,[33] this patient's parents should be educated on how to recognize these and initiate appropriate care for their child. Children with AD are also at high risk of developing AR or asthma in later life,[32] so family education should encompass the signs and symptoms of these as well, with an emphasis on the importance of seeking professional care promptly.

CONCLUSIONS

Allergic disease has a profound and long-lasting impact on overall health, safety, and quality of life. Fortunately, recent advances in treatment now allow most patients to achieve good-to-excellent symptom control with minimal side effects. The keys to effective care are early and accurate diagnosis, a strong emphasis on allergen avoidance, and a flexible, multifaceted approach to drug therapy. Because allergy treatment is usually needed for many years or even a lifetime, it should be designed with special attention to long-term efficacy, safety, tolerability, patient acceptability, affordability, and cost-effectiveness. These goals are best achieved using a team approach that includes the primary care physician, specialists in allergic disease, and allied health professionals such as nurses, nutritionists, and pharmacists as well as patients and their families.

FIGURE 3

Freedom From AD Flares in Children Treated for 12 Months With Pimecrolimus (a Topical Calcineurin Inhibitor) or Conventional Emollient Therapy. Significant Advantages for Pimecrolimus Were Observed Regardless of Baseline Disease Severity



Adapted with permission from Wahn U, et al. *Pediatrics*. 2002;110:1-80.

REFERENCES

1. Juniper EF, Guyatt GH, Dolovich J. Assessment of quality of life in adolescents with allergic rhinoconjunctivitis: development and testing of a questionnaire for clinical trials. *J Allergy Clin Immunol*. 1994;93:413-423.
2. Borres MP, Brakenhielm G, Irander K. How many teenagers think they have allergic rhinoconjunctivitis and what they do about it. *Ann Allergy Asthma Immunol*. 1997;78:29-34.
3. Meltzer EO. Quality of life in adults and children with allergic rhinitis. *J Allergy Clin Immunol*. 2001;108:S45-53.
4. Tanner LA, Reilly M, Meltzer E, Bradford JE, Mason J. Effect of fexofenadine HCl on quality of life and work, classroom, and daily activity impairment in patients with seasonal allergic rhinitis. *Am J Manag Care*. 1999;5:S235-S347.
5. American Academy of Allergy, Asthma & Immunology. Rhinitis. In: The Allergy Report: Diseases of the Atopic Diathesis. Available at: http://www.theallergyreport.org/professional/rhinitis 0.html. Accessed December 2, 2003.
6. Craig TJ, Teets S, Lehman EB, Chinchilli VM, Zwillich C. Nasal congestion secondary to allergic rhinitis as a cause of sleep disturbance and daytime fatigue and the response to topical nasal corticosteroids. *J Allergy Clin Immunol*. 1998;101:633-637.
7. Vuurman EFPM, van Veggel LMA, Uiterwijk MMC, Leutner D, O'Hanlon JF. Seasonal allergic rhinitis and antihistamine effects on children's learning. *Ann Allergy*. 1993;71:121-126.
8. Berger WE, Schenkel EJ, Mansfield LE. Safety and efficacy of desloratadine 5 mg in asthma patients with seasonal allergic rhinitis and nasal congestion. *Ann Allergy Asthma Immunol*. 2002;89:485-491.
9. Spector SL, Nicodemus CF, Corren J, et al. Comparison of the bronchodilatory effects of cetirizine, albuterol, and both together versus placebo in patients with mild-to-moderate asthma. *J Allergy Clin Immunol*. 1995;96:174-181.
10. Nathan RA. Pharmacotherapy for allergic rhinitis: a critical review of leukotriene receptor antagonists compared with other treatments. *Ann Allergy Asthma Immunol*. 2003;90:1-10.
11. Malmstrom K, Hampel FC, Philip G, Malice MP, Reiss TF. Montelukast in the treatment of Spring allergic rhinitis in a large, double-blind, randomized, placebo-controlled study. *J Allergy Clin Immunol*. 2001;107:S157.
12. Wilson AM, Orr LC, Coutie WJ, Sims EJ, Lipworth BJ. A comparison of once daily fexofenadine versus the combination of montelukast plus loratadine on domiciliary nasal peak flow and symptoms in seasonal allergic rhinitis. *Clin Exp Allergy*. 2002;32:126-132.
13. Storms WW. Rethinking our approach to allergic rhinitis management. *Ann Allergy Asthma Immunol*. 2002;88(suppl):30-35.
14. Mandl M, Nolop K, Lutsky BN. Comparison of once daily mometasone furoate (Nasonex) and fluticasone propionate aqueous nasal sprays for the treatment of perennial rhinitis. 194-079 Study Group. *Ann Allergy Asthma Immunol*. 1997;79:370-378.
15. Drouin M, Yang WH, Bertrand B, et al. Once daily mometasone furoate aqueous nasal spray is as effective as twice daily beclomethasone dipropionate for treating perennial allergic rhinitis patients. *Ann Allergy Asthma Immunol*. 1996;77:153-160.
16. Schenkel EJ, Skoner DP, Bronsky EA, et al. Absence of growth retardation in children with perennial allergic rhinitis after one year of treatment with mometasone furoate aqueous nasal spray. *Pediatrics*. 2000;105:E22.
17. Skoner DP, Rachelefsky GS, Meltzer EO, et al. Detection of growth suppression in children during treatment with intranasal beclomethasone dipropionate. *Pediatrics*. 2000;105:E23.
18. Airway remodeling in asthma: do histological changes and functional changes correlate? *Medical Crossfire*. 2002;4:35-47.
19. Sussman GL, Mason J, Compton D, Stewart J, Ricard N. The efficacy and safety of fexofenadine HCl and pseudoephedrine, alone and in combination, in seasonal allergic rhinitis. *J Allergy Clin Immunol*. 1999;104:100-106.
20. Berkowitz RB, Woodworth GG, Lutz C, et al. Onset of action, efficacy, and safety of fexofenadine 60 mg/pseudoephedrine 120 mg versus placebo in the Atlanta allergen exposure unit. *Ann Allergy Asthma Immunol*. 2002;89:38-45.
21. Creticos PS. The consideration of immunotherapy in the treatment of allergic asthma. *Ann Allergy Asthma Immunol*. 2001;87:13-27.
22. Möller C, Dreborg S, Ferdousi HA, et al. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study). *J Allergy Clin Immunol*. 2002;109:251-256.
23. Turjanmaa K, Alenius H, Makinen-Kiljunen S, Reunala T, Palosuo T. Natural rubber latex allergy. *Allergy*. 1996;51:593-602.
24. Allmers H, Schmengler J, Skudlik C. Primary prevention of natural rubber latex allergy in the German health care system through education and intervention. *J Allergy Clin Immunol*. 2002;110:318-323.
25. Charous BL, Blanco C, Tarlo S, et al. Natural rubber latex allergy after 12 years: recommendations and perspectives. *J Allergy Clin Immunol*. 2002;109:31-34.
26. Allmers H, Brehler R, Chen Z, Raulf-Heimsoth M, Fels H, Baur X. Reduction of latex aeroallergens and latex-specific IgE antibodies in sensitized workers after removal of powdered natural rubber latex gloves in a hospital. *J Allergy Clin Immunol*. 1998;102:841-846.
27. Tarlo SM, Easty A, Eubanks K, et al. Outcomes of a natural rubber latex control program in an Ontario teaching hospital. *J Allergy Clin Immunol*. 2001;108:628-633.
28. Freeman GL. Co-occurrence of latex and fruit allergies. *Allergy Asthma Proc*. 1997;18:85-88.
29. Weiss SJ, Halsey JF. A nurse with anaphylaxis to stone fruits and latex sensitivity: potential diagnostic difficulties to consider. *Ann Allergy Asthma Immunol*. 1996;77:504-508.
30. Kim KT, Hussain H. Prevalence of food allergy in 137 latex-allergic patients. *Allergy Asthma Proc*. 1999;20:95-97.
31. Larsen FS, Hanifin JM. Epidemiology of atopic dermatitis. *Immunol Allergy Clin N Am*. 2002;22:1-24.
32. Leung DYM. Atopic dermatitis: new insights and opportunities for therapeutic intervention. *J Allergy Clin Immunol*. 2000;105:860-876.
33. Laughter D, Istvan JA, Tofte SJ, Hanifin JM. The prevalence of atopic dermatitis in Oregon schoolchildren. *J Am Acad Dermatol*. 2000;43:649-655.
34. Grewe M, Bruijnzeel-Koomen CA, Schopf E, et al. A role for Th1 and Th2 cells in the immunopathogenesis of atopic dermatitis. *Immunol Today*. 1998;19:359-361.
35. Ong PY, Hamid QA, Travers JB, et al. Decreased IL-15 may contribute to elevated IgE and acute inflammation in atopic dermatitis. *J Immunol*. 2002;168:505-510.
36. Remitz A, Kyllonen H, Granlund H, Reitamo S. Tacrolimus ointment reduces staphylococcal colonization of atopic dermatitis lesions. *J Allergy Clin Immunol*. 2001;107:196-197.
37. Wahn U, Bos JD, Goodfield M, et al. Efficacy and safety of pimecrolimus cream in the long-term management of atopic dermatitis in children. *Pediatrics*. 2002;110:e2.

Interdisciplinary Medicine®
8

CASE STUDIES IN ALLERGIC DISEASE: KEY DECISION POINTS IN DIAGNOSIS AND TREATMENT

CME Credit Information and Post Test Assessment

The estimated time to read the newsletter and complete the Post Test is 1 hour.

Release date: October 2003 — Expiration date: October 2004

PHYSICIANS

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of National Jewish Medical and Research Center and IMED Communications. National Jewish Medical and Research Center is accredited by the ACCME to provide continuing medical education for physicians.

National Jewish Medical and Research Center designates this educational activity for up to 1 category 1 credit towards the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the activity.

Instructions:

To apply for AMA PRA category 1 credit, you must

- Complete the Post Test and Evaluation Form
- Mail your completed form to

Office of Professional Education
National Jewish Medical and Research Center
1400 Jackson Street
Room G107
Denver, CO 80206 **Or** fax to 1-800-530-7940

NURSES AND NURSE PRACTITIONERS

National Jewish Medical and Research Center is Provider approved by the California Board of Registered Nursing, Provider Number CEP 12724, for 1.0 contact hours.

Instructions:

To apply for contact hours, you must:

- Complete the Post Test and Evaluation Form
- Mail your completed form to

National Jewish Medical and Research Center
1400 Jackson Street
Room M-319
Denver, CO 80206 **Or** fax to 1-800-530-7940

PHYSICIAN ASSISTANTS

This program has been reviewed and is approved for a maximum of 1 hour of clinical Category I (Preapproved) CME credit by the Physician Assistant Review Panel. Approval is valid for 1 year from the issue date of October 2003. Participants may submit the self-assessment at any time during that period.

This program was planned in accordance with AAPA's CME Standards for Enduring Material Programs and for Commercial Support of Enduring Material Programs.

Successful completion of the self-assessment is required to earn Category I (Preapproved) CME credit. Successful completion is defined as a cumulative score of at least 70% correct.

Instructions:

To receive CME credit, Physician Assistants should submit this Post Test online. You will get immediate feedback and can print your certificate of completion right away. (70% correct required for credit.) Sign onto the AAPA website at www.aapa.org and go to the CME services section. Click on the link to "Post Tests Online."

POST TEST

1. In children with AR, which antihistamine has been shown to worsen academic performance more than the allergy symptoms themselves do?
   a. Loratadine
   b. Fexofenadine
   c. Desloratadine
   d. Diphenhydramine

2. For severe, persistent symptoms of AR, the ARIA guidelines recommend first-line treatment with:
   a. An oral H_1 antihistamine
   b. An intranasal corticosteroid
   c. An antileukotriene receptor antagonist
   d. None of the above

3. Immunotherapy is effective in controlling AR symptoms caused by:
   a. Animal dander
   b. Dust mites
   c. Pollen
   d. All of the above

4. Anaphylaxis is more likely to be fatal to asthmatic than to nonasthmatic individuals.
   a. True
   b. False

5. Latex allergy frequently coexists with allergies to:
   a. Dairy foods
   b. Tree nuts
   c. Fruits
   d. Shellfish

6. In addition to epinephrine for treating anaphylaxis, the clinician should consider:
   a. Oxygen
   b. An antihistamine
   c. Both a and b
   d. Neither a nor b

7. The onset of AD usually occurs:
   a. In infancy
   b. In adolescence
   c. In early adulthood
   d. In late adulthood

8. Some cases of AD are believed to represent abnormal cutaneous responses to:
   a. *Escherichia coli*
   b. *Staphylococcus aureus*
   c. *Streptococcus pneumoniae*
   d. *Streptococcus viridans*

9. Topical calcineurin inhibitors are associated with which steroid-type side effect?
   a. Growth inhibition
   b. Skin atrophy
   c. Cataracts
   d. None of the above

10. Children with AD are prone to developing what conditions in later life?
    a. Chronic xerosis and hand dermatitis
    b. AR and asthma
    c. Both a and b
    d. Neither a nor b

Answer key
1.d 2.b 3.d 4.a 5.c 6.c 7.a 8.b 9.d 10.c

03AVP02B

Printed in the USA

36471

CONTINUING EDUCATION POST TEST

Current Trends in Allergic Disease: Key Decision Points in Diagnosis and Treatment

1.	○ a	○ b	○ c	○ d	5.	○ a	○ b.	○ c.	○ d.
2.	○ a.	○ b.	○ c.	○ d.	7	○ a.	○ b.	○ c.	○ d
3.	○ a	○ b	○ c.	○ d.	8	○ a.	○ b.	○ c.	○ d.
4.	○ a.	○ b.	○ c.	○ d.	9	○ a.	○ b.	○ c.	○ d
6	○ a	○ b	○ c.	○ d	10	○ a	○ b	○ c	○ d

Program Evaluation

Your frank evaluation of this activity will be helpful in improving our continuing education programs. We hope this newsletter has provided information that will be useful in your practice. Please evaluate the newsletter by answering the following questions.

1 How would you rate	Superior	Excellent	Good	Fair	Poor
a. Value of the topic	○	○	○	○	○
b Relevance to your practice	○	○	○	○	○
c. Quality of information	○	○	○	○	○

2. Did this material succeed in meeting its educational objectives? ○ Yes ○ No

3 Will reading this newsletter change the way in which you treat patients? ○ Yes ○ No

4. Do you believe the newsletter contained pharmaceutical industry bias? ○ Yes ○ No

5. When information is presented by a federal healthcare agency (i.e. NIH, DHHS, CDC), does it increase the likelihood that you will read it? ○ Yes, definitely ○ Neutral ○ No, no change

6 How do you prefer to receive continuing medical education information?	Very Useful	Somewhat Useful	Don't Use
a Newsletter	○	○	○
b. Monograph	○	○	○
c. Symposium/Conference	○	○	○
d. Journal articles	○	○	○
e. Teleconference	○	○	○
f. CD-ROM/Audio and/or video	○	○	○
g Internet	○	○	○

7. Actual amount of time I spent on this activity [ ][ ] . [ ][ ] Hours

Last Name

First Name

Middle Initial ○ MD ○ DO ○ RN ○ NP ○ PA Specialty

Company

Address

City State Zip

Phone - - Fax - -

Email

For contact hours fill in this line State License # Date / /

To receive your certificate, fax this completed sheet to 1-800-530-7940.

Editor: ***Interdisciplinary Medicine***®
IMED Communications
Dept 102
518 Route 513, Suite 200
PO Box 458
Califon, NJ 07830

PRSRT
STD
US Postage
PAID
A&E Mailers

Interdisciplinary Medicine®

Case Studies in Allergic Disease:
Key Decision Points in Diagnosis and Treatment

Vol. 5 No. 3

IMPORTANT CME MATERIALS ENCLOSED

Developed by IMED Communications for
National Institute of Allergy and Infectious Diseases, National Institutes of Health, U.S. Department of Health and Human Services; and
National Jewish Medical and Research Center

In cooperation with AAAAI, AANP, AAOA, AAPA, ACAAI, ACOEM, AMA, APA, and NAMCP
This program is supported by an unrestricted educational grant from Aventis Pharmaceuticals.